

is possible that some forms of RP might be different diseases even with a common inheritance pattern.<sup>12</sup>

The probably normal plasmatic transport of retinol in RP does not obviously rule out the possibility that a defect of vitamin A metabolism is at the root of some form of RP. Nothing is known of the intimate mechanism by which retinol is utilized by the pigment and neuroepithelium of the retina. It is clear that only a better knowledge of this basic point at the molecular level in normal and RP eyes will help settle the question whether or not a local disturbance of retinol metabolism is of any importance in this disease.

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**Key words:** retinol-binding protein, vitamin A, retinitis pigmentosa of different genetic type.

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#### Blood pressure and pressure amaurosis.

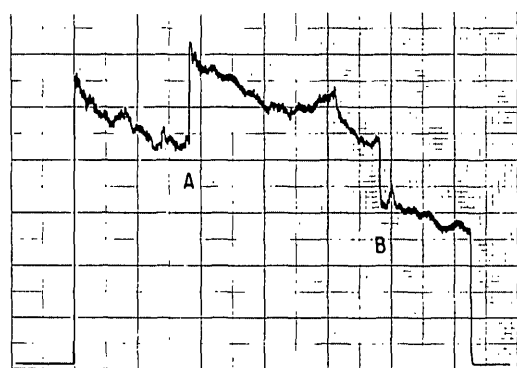
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*Susceptibility to pressure amaurosis was measured in young research subjects before and during blood pressure elevation induced by intravenous infusions of phenylephrine. Intraocular pressure elevations were produced by paralimbal suction; we measured the highest level to which intraocular pressure could be raised without obliterating perception of a slowly flickering stimulus in the nasal field of vision. Elevation of systemic blood pressure was accompanied in all subjects by a corresponding increase in the highest "safe" level of intraocular pressure. This observation confirms the commonly held hypothesis that pressure amaurosis is the result of pressure-induced neuroretinal ischemia.*

Pressure amaurosis is a sudden loss of vision occurring a few seconds after a marked elevation of intraocular pressure. Depending upon how high the pressure is raised, the amaurosis may be partial or complete. Certain parts of the visual field, including the Bjerrum region,<sup>1-3</sup> the pericentral area,<sup>4-6</sup> the nasal field,<sup>7</sup> and the far periphery,<sup>6, 8</sup> lose vision at pressure elevations insufficient to cause amaurosis in the remaining central and temporal portions of the field. Because early loss of vision from glaucoma typically occurs in the same pressure-sensitive areas of the visual field, it is possible that the mechanism for visual loss in pressure amaurosis and glaucoma are similar.

An ischemic mechanism for pressure amaurosis is implied by several observations. First, in order to induce amaurosis, intraocular pressure must be raised to near the diastolic ophthalmic artery pressure.<sup>3, 7</sup> Second, individuals with high ophthalmic artery pressures are, in general, less susceptible to pressure amaurosis than are individuals with low ophthalmic artery pressures.<sup>2, 6, 9</sup> Finally, the blackout of vision in pressure amaurosis resembles that which occurs with postural hypotension or during positive acceleration in aviators, two conditions which transiently lower ophthalmic artery pressure.

These observations do not necessarily exclude the possibility of a nonischemic mechanism. For example, high intraocular pressure might direct-



**Fig. 1.** The effect of paralimbal suction on intraocular pressure. Suction was applied at A and released at B. Intraocular pressure is being monitored by a conventional electronic Schiøtz tonometer; thus, the decay in intraocular pressure is much greater than that occurring with only suction applied to the eye.

**Table I.** Consistency of Px and blood pressure relationship upon repeated measurements

Subject	BP (mm. Hg)	Px (mm. Hg)	BP-Px (mm. Hg)
A	99	62	37
A	98	61	37
A	94	60	36
B	80	47	33
B	81	48	33
B	93	57	36
C	79	51	28
C	81	49	32
C	64	39	25
D	89	48	41
D	89	48	41
D	87	48	39

Px = Highest intraocular pressure at which test stimulus remains visible.

BP = Mean brachial artery blood pressure.

ly compress nerve fibers or distort their course through the cribriform plate, thus interfering with transmission of nerve impulses or with axoplasmic flow.

In this study we wished to obtain conclusive evidence for or against an ischemic mechanism for pressure amaurosis. Specifically, we proposed to determine whether or not raising an individual's blood pressure would alter his susceptibility to pressure amaurosis.

**Methods.** We raised intraocular pressure in the right eyes of young healthy subjects with a Smith, Miller, and Patch semi-automated suction ophthalmodynamometer. Suction was applied through an 11 mm. cup positioned over sclera just temporal to the limbus. We could preset the desired level of suction and instantaneously transfer it to the eye, causing an abrupt rise in intraocular pressure (Fig. 1).

The subjects were seated at an Oculus (Tubingen) perimeter and pre-adapted to a background illumination of 10 asb. A red, 30', 1000 asb. fixation light was used. We monitored perception at a single visual field point, 20° nasal to fixation and 5° above the horizontal meridian. The test stimulus light was white and 10' in diameter. It was set to slowly flicker at a frequency of 2 Hz. in order to overcome the Troxler effect of local adaptation; frequent blinking was also encouraged for the same purpose. A suprathreshold stimulus of 1,000 asb. was used after preliminary experiments showed that varying the stimulus intensity affected the measurement only if the intensity was very close to threshold; at such low stimulus intensities the subject's endpoint decisions became difficult and imprecise.

We determined the highest elevation of intraocular pressure at which the test stimulus remained perceptible. Our general procedure was to apply to the eye a predetermined amount of suction, have the subject measure by stopwatch the time until the stimulus disappeared, and then release the suction. We repeated this maneuver several times, each time decreasing the amount of suction by 5 mm. of vacuum (equivalent to a decrement in intraocular pressure of 2 to 3 mm. Hg), until a level was reached at which the test stimulus remained visible for at least 60 seconds. Upon reaching this endpoint, we turned the subject to an adjacent slit lamp and, with the suction reapplied at the critical level, measured his intraocular pressure (Px) with a Goldmann applanation tonometer. Mean systemic blood pressure (diastolic blood pressure +  $\frac{1}{3}$  {systolic blood pressure - diastolic blood pressure}) was measured before and after each test run. If the two measurements differed, the results were averaged.

To evaluate how alterations of blood pressure might affect susceptibility to pressure amaurosis, we measured Px in six subjects under each of the following conditions: (1) control, with intravenous infusion of normal saline; (2) after intravenous injection of atropine sulfate, 1 mg.; (3) during a constant intravenous infusion of phenylephrine HCl, 0.1  $\mu$ g per kilogram per minute, preceded by an intravenous injection of atropine sulfate, 1 mg.; and (4) during a constant intravenous infusion of phenylephrine HCl, 1.0  $\mu$ g per kilogram per minute, preceded by an intravenous injection of atropine sulfate, 1 mg.

Phenylephrine was infused through a constant infusion pump. Reflex bradycardia made the phenylephrine-induced blood pressure elevation unstable unless atropine was given first. Blood pressure was measured every minute during the infusion. Subjects were unaware of whether saline or phenylephrine was being infused; the symptoms of atropinization could not be masked.

**Table II.** Effect of atropine and phenylephrine on BP and Px (Mean  $\pm$  S.E.)

	BP (mm. Hg)	Px (mm. Hg)	BP-Px (mm. Hg)
Control	83.3 $\pm$ 4.5	51.3 $\pm$ 3.2	32.0 $\pm$ 2.4
Atropine	87.8 $\pm$ 1.7	54.0 $\pm$ 2.5	33.8 $\pm$ 2.1
Phenylephrine, 0.1 $\mu$ g/Kg./min., + atropine, 1 mg.	103.3 $\pm$ 4.8	70.8 $\pm$ 6.5	32.5 $\pm$ 3.5
Phenylephrine, 1.0 $\mu$ g/Kg./min., + atropine, 1 mg.	112.2 $\pm$ 1.6	77.2 $\pm$ 2.4	35.0 $\pm$ 1.8

Tukey's multiple comparison treatment was used to evaluate the statistical significance of observed changes in BP and Px.

**Results.** With observer practice, the endpoint (Px) became very sharp. Amaurosis was an all-or-none phenomenon, occurring either within four to five seconds or not at all, depending on the height of the intraocular pressure. At Px, the brightness of the test stimulus waxed and waned in phase with respiration.

Table I lists Px and mean systemic blood pressure (BP) of four subjects, each tested three times on different days. Although Px varied slightly in two of the subjects from day-to-day, the BP-Px difference was remarkably constant for each individual.

Pharmacologic manipulation of blood pressure produced similar effects on BP and Px in all six subjects (Table II). Atropine, when given alone, caused no alteration of either measurement. Phenylephrine infusion, on the other hand, produced moderate elevations of both BP and Px ( $p < 0.01$  for each concentration of phenylephrine). The elevations of BP and Px were greater during infusion of the more concentrated solution of phenylephrine; however, this tendency toward a dose-related response to phenylephrine was not statistically significant. The increases of BP and Px during phenylephrine infusion were nearly equal; thus the difference between the two pressures (BP-Px) did not change.

No adverse ocular or systemic effects were produced by the testing procedures.

**Discussion.** Our experiment was designed to prove or disprove an ischemic mechanism for pressure amaurosis. We reasoned that if pressure amaurosis were the result of a direct nonischemic action of high intraocular pressure on neuronal function, phenylephrine-induced alterations in systemic blood pressure would not influence susceptibility to pressure amaurosis. We found the opposite to be true. The higher we raised systemic blood pressure, the higher we needed to raise intraocular pressure to induce amaurosis.

There is a remote possibility that phenylephrine itself might, in some unrecognized manner, directly influence pressure sensitivity of neural tissue. However, such a neurotropic effect is not one of the known pharmacologic actions of phenylephrine; an indirect effect mediated through the blood pressure seems much more likely.

Do the results of this experiment illuminate the pathogenesis of chronic glaucomatous optic nerve damage? A close relationship between pressure amaurosis and glaucomatous visual loss is suggested by several obvious similarities. Both conditions result from an abnormally high intraocular pressure. Both appear to preferentially affect the nasal and paracentral areas of the visual field (although the exact pattern of regional variations in susceptibility to pressure amaurosis requires further elucidation). Finally, abundant clinical evidence suggests that the susceptibility of an optic nerve to glaucomatous damage, like its susceptibility to pressure amaurosis, depends upon the level of systemic blood pressure.<sup>10</sup>

However, several equally obvious differences between the two phenomena temper one's enthusiasm for concluding that their pathogeneses are the same. Loss of vision from pressure amaurosis is temporary; loss of vision from glaucoma is usually permanent. Pressure amaurosis is sudden, occurring within a few seconds; glaucomatous loss of vision occurs slowly, often requiring months or years. Extremely high intraocular pressures are necessary to produce pressure amaurosis; the intraocular pressures in chronic glaucoma are usually much lower.

Thus the results of our experiment and of any others involving an acute marked elevation of intraocular pressure should be interpreted with caution. Information gained from acute experiments may or may not be relevant to the pathogenesis of glaucomatous optic atrophy. The similarities between pressure amaurosis and glaucoma do encourage further experiments to test how the two phenomena are related.

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**Key words:** intraocular pressure, suction cup, blood pressure, amaurosis, glaucoma.

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**Lymphocyte-induced vitreous membranes: a comparative study with leukocyte- and platelet-induced vitreous membranes.**

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*Vitreous membranes were induced in rabbit eyes by injecting an autogenous lymphocyte preparation. These membranes were compared with membranes induced by autogenous leukocyte and platelet preparations. Lymphocytes gave rise to faint, nonprogressive membranes, while leukocytes and platelets produced dense, long-standing membranes. It is suggested that lymphocytes may not be the cause of this weak response, as other cells in the preparation may be involved.*

In 1966, Freilich, Lee, and Freeman<sup>1</sup> injected autogenous whole blood into rabbit eyes. Mem-

branes appeared in all eyes receiving two blood injections spaced at an interval of six weeks, and in five of 24 eyes receiving only one injection. Vitreous membranes have also been produced by the injection of partially purified blood components. Lam, Ashrafzadeh, and Lee<sup>2</sup> produced dense vitreous membranes one week after the injection of leukocytes. Constable and co-workers<sup>3</sup> induced membranes with platelet-rich plasma. Red blood cells may also have a role in the formation of vitreous membrane.<sup>2</sup>

The present study reports the production of vitreous membranes with a lymphocyte preparation and compares them with membranes produced with leukocyte and platelet preparations.

**Preparation of cells.** Leukocytes, lymphocytes, and platelets were prepared from autogenous blood as described previously.<sup>1-5</sup> There was less than 1 per cent red cell contamination and no platelet contamination in the leukocyte preparation. The lymphocyte preparation consisted of 90 per cent small lymphocytes. Cell concentrations, measured by a hemocytometer count of at least 400 cells per sample, were adjusted to correspond to normal blood:  $1 \times 10^6$  cells per milliliter for lymphocytes and  $1 \times 10^9$  cells per milliliter for platelets, suspended in saline.

**Injection of cells.** Adult pigmented and albino rabbits were anesthetized with intravenous sodium pentobarbital (30 mg. per kilogram). The fundus was examined with the indirect ophthalmoscope. Using aseptic techniques, 0.1 ml. of the cell preparation was injected with a tuberculin syringe with a 27-gauge needle into the vitreous cavity through the pars plana ciliaris 4 mm. behind the limbus. The injection was located in the central vitreous by guiding the needle tip with indirect ophthalmoscopy, which was also used to observe the fundus after the injection.

A total of 63 eyes were injected: 36 with lymphocytes, 13 with platelets, and 14 with leukocytes. Fewer leukocyte and platelet injections were performed, since they have been studied previously<sup>3,4</sup> and were only intended for comparative purposes. Normal saline was injected into the vitreous cavity of ten eyes as a control.

**Examination.** Follow-up examination of the injected eyes was performed daily during the first week after injection and then at weekly intervals for eight months (263 days). Examination included biomicroscopy and indirect ophthalmoscopy. Visible vitreous membranes were photographed with a portable Kowa fundus camera.

**Histopathology.** All eyes were eventually enucleated at different time intervals and the membranes removed. The eyes were washed thoroughly with water to avoid contamination by blood. The globe was sectioned at the equator with a sharp razor blade and scissors. The exposed vitreous was searched for membranes with a